1 Introduction

Diabetes is currently one of the major causes of morbidity and mortality in the world. The number of diabetic patients is markedly increasing in both developed and developing countries. According to the World Health Organization reports (October, 2013), 347 million people have diabetes worldwide. It is estimated that 3.4 million patients died from consequences of hyperglycemia in the year 2004; without urgent action, diabetes will be the 7th cause of mortality in 2030. This disease occurs either when β-islet cells do not produce enough insulin (type 1 diabetes mellitus, T1DM) or when the tissues become resistant to insulin (type 2 diabetes mellitus, T2DM)[1].

Both types of diabetes can damage nerves and blood vessels in different tissues and lead to serious complications. Therefore, over time, macrovascular complications like cardiovascular diseases and microvascular complications, such as neuropathy, nephropathy and retinopathy, occur in poorly controlled patients[3][4]. Insulin and oral hypoglycemic drugs, including insulin sensitizers, insulin secretagogues, α-glucosidase inhibitors, incretin agonists and dipeptidyl peptidase-4 inhibitors, are the most widely used drugs for...
management of diabetes. However, their clinical uses are limited due to their unpleasant side effects, such as lactic acidosis, peripheral edema and abdominal discomfort\(^{[25]}\). Therefore, the search for antidiabetic agents with lesser side effects and greater effectiveness is still of great interest.

Numerous herbs have been reported to possess antidiabetic effects. Many of these herbs have been shown to have hypoglycemic effects in animal studies or clinical trials\(^{[1-6]}\). Also, a number of them, such as Panax quinquefolius, Morus alba and Cinnamomum cassia, provide diabetes treatment so effective that their formulations have been approved in different countries as antidiabetic agents\(^{[7]}\). It is believed that herbal formulations containing multiple plants can have greater effects than the same herbs taken separately. These synergistic effects enhance the desired action\(^{[8]}\). Based on this belief, several polyherbal formulations have been studied as therapeutic agents for the control of diabetes. The current review focuses on effects of these polyherbal formulations on blood glucose, lipids and other biochemical parameters. It also compares their antidiabetic effects, using oral hypoglycemic drugs as reference.

2 Literature search

A literature search was conducted through the Google Scholar, MEDLINE and Scopus databases, which cover the most important and influential peer-reviewed articles. The search included literature published as late as 31 January 2014, and used Medical Subject Heading terms “diabetes”, “formulation”, “glucose”, “herb” and “medicinal plant”. Only herbal products prepared from at least two herbs were incorporated in the review. In some animal studies, effects of polyherbal supplements have not been compared with a standard antidiabetic drug. Results of these works have not been included in this paper. Also excluded from this review were studies that did not define constituents of polyherbal products and studies that did not report data in such a way that percent of effectiveness of products could be calculated.

3 Current status of polyherbal formulations

At least 16 polyherbal products have been tested for their beneficial effects on biochemical parameters of diabetic rodents. These products are listed in Table 1\(^{[9-24]}\). All products except of Karnim Plus, 5EPHF, Diakyr, DRF/AV/5001 and HAL, produced greater reduction in fasting blood glucose (FBG) than the reference drug used in that study. These drugs included glibenclamide, acarbose, rosiglitazone, pioglitazone, metformin and tolbutamide. Also, with the exception of DRF, all polyherbal formulations showed better effect on glycosylated hemoglobin (HbA\(_1c\)) level compared with reference drugs. Interestingly, all herbal products tested were better at increasing serum insulin level than the reference drugs. Of the formulations tested, Glyoherb showed the greatest reduction in FBG (75% decrease) and Cogent db showed the greatest increase in insulin (104% increase).

The antihyperglycemic effect of herbs can be achieved by many mechanisms, such as inhibiting glucose absorption in the intestine, enhancing insulin secretion from the pancreas, increasing glucose uptake by tissues, decreasing glucose production in the liver, increasing pancreatic tissue regeneration\(^{[25-28]}\). Since polyherbal compounds contain so many ingredients from different herbs, it is difficult to identify the exact mechanism of their action on hypoglycemia. It is likely that the antihyperglycemic effect of a polyherbal compound is achieved through various mechanisms. For example, Diasulin contains both Cassia auriculata and Gymnema sylvestre, which decrease blood glucose by inhibiting glucose absorption from the intestine and enhancing insulin secretion from the pancreas, respectively\(^{[29,30]}\). In addition, the presence of Trigonella foenum-graecum in this compound may induce hypoglycemia by enhancing insulin secretion, increasing glucose uptake by tissues, decreasing glucose absorption from the intestine and inhibiting glucose production in hepatocytes\(^{[31-33]}\).

Diabetic dyslipidemia, which is often present in diabetic patients, is one of the main risk factors for cardiovascular diseases. It is characterized by an elevation in serum triglyceride and low-density lipoprotein (LDL) levels accompanied by a decrease in high-density lipoprotein (HDL) concentration\(^{[34-37]}\). According to current guidelines, decreasing serum LDL concentration is the primary goal for management of diabetic dyslipidemia. Yet, despite forceful drug therapy, most diabetic patients do not reach the advised LDL concentration (<100 mg/dL)\(^{[37,38]}\). Among all the products listed in Table 1, only Karnim Plus, HAL, MAC-ST/001 and Cognet db failed to show greater hypolipidemic effect than reference drugs. Therefore, the herbal products have beneficial effects on lipid profile of diabetic rodents and they have the potential to be used as alternative or complementary agents for treatment of diabetic dyslipidemia.

Table 2\(^{[39-43]}\) shows four polyherbal formulations that demonstrated antidiabetic effects in clinical trials on diabetic patients. Three of four compounds induced considerable hypoglycemic effects. However, none of the trials used insulin or any oral hypoglycemic drugs as control and therefore it is not possible to compare hypoglycemic action of these polyherbal compounds with that of a reference drug. Only Viswanathan et al\(^{[42]}\) compared beneficial effects of their formulation on diabetic foot ulcer with silver sulphadiazine cream.

Analysis of constituents of the polyherbal products listed in Table 1 and Table 2 shows that Momordica charantia,
Table 1 (to be continued) Polyherbal formulations that have been tested in animal studies for management of diabetes

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Polyherbal preparation name</th>
<th>Herbal constituents</th>
<th>Study design</th>
<th>Effects of polyherbal preparation (% of change)</th>
<th>Effects of reference drug (% of change)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Babu et al, 2004</td>
<td>Hyponidd</td>
<td><em>Cassia auriculata</em>, <em>Curcuma longa</em>, <em>Emblica officinalis</em>, <em>Enicostemma littorale</em>, <em>Eugenia jambolana</em>, <em>Gymnema sylvestre</em>, <em>Melia Azadirachta</em>, <em>Momordica charantia</em>, <em>Pterocarpus marsupium</em>, <em>Tinospora cordifolia</em></td>
<td>STZ-induced diabetic rats; feeding of 100 or 200 mg/kg daily for 45 d</td>
<td>At 200 mg/kg: ↓FBG (72%) ↑Insulin (96%) ↑HbA1c (47%) ↑Hepatic glycogen (77%) ↓Hepatic glycogen (77%) ↑Oxidative stress (plasma)</td>
<td>Glibenclamide (600 µg/kg): ↓FBG (69%) ↑Insulin (79%) ↑HbA1c (41%) ↑Hepatic glycogen (68%) ↓Oxidative stress (plasma)</td>
</tr>
<tr>
<td>Pari et al, 2002</td>
<td>Cogent db</td>
<td><em>Azadirachta indica</em>, <em>Curcuma longa</em>, <em>Phyllanthus emblica</em>, <em>Rotula aquatic</em>, <em>Syzygium cumini</em>, <em>Terminalia bellerica</em>, <em>Tribulus terrestris</em>, <em>Trigonella foenum graecum</em></td>
<td>Alloxan-induced diabetic rats; feeding of aqueous solution (0.15–0.45 g/kg daily) for 40 d</td>
<td>At 0.45 g/kg: ↓FBG (64%) ↑Insulin (104%) ↑HC (31%) ↑TG (25%) ↑HDL (47%) ↓Glucosuria ↑Glucose tolerance</td>
<td>Glibenclamide (600 µg/kg): ↓FBG (60%) ↑Insulin (87%) ↑TC (31%) ↑TG (28%) ↑HDL (29%) Glucose tolerance</td>
</tr>
<tr>
<td>Saravanan et al, 2005</td>
<td>Diasulin</td>
<td><em>Cassia auriculata</em> (flower), <em>Coccinia indica</em> (fruit), <em>Curcuma longa</em> (rhizome), <em>Emblica officinalis</em> (fruit), <em>Gymnema sylvestre</em> (leaf), <em>Momordica charantia</em> (fruit), <em>Scoparia dulcis</em> (whole plant), <em>Syzygium cumini</em> (seed), <em>Tinospora cardifolia</em> (root), <em>Trigonella foenum-graecum</em> (seed)</td>
<td>Alloxan-induced diabetic rats; feeding of alcoholic extract (200 mg/kg daily) for 30 d</td>
<td>↓FBG (60%) ↑Glucose tolerance</td>
<td>Glibenclamide (600 µg/kg): ↑FBG (58%) ↑Insulin (78%) ↓Tissue lipids in the liver and kidney</td>
</tr>
<tr>
<td>Chang et al, 2006</td>
<td>Okchun-San</td>
<td><em>Coix lachryma-jobi</em> (Oryza sativa), <em>Glycyrrhiza uralensis</em>, <em>Puergia thunbergiana</em>, <em>Rehmannia glutinosa</em>, <em>Schizandra chinensis</em>, <em>Trichosanthes kirilowii</em></td>
<td><em>db/db</em> type-2 diabetic mice; feeding of aqueous extract (200 mg/kg daily) for 12 d</td>
<td>↓FBG (&lt;60%) ↑Glucose tolerance</td>
<td>Glibenclamide (600 µg/kg): ↑FBG (42%) ↑Insulin (86%) ↓Histological damage in the pancreas</td>
</tr>
<tr>
<td>Mandlik et al, 2008</td>
<td>DRF/AY/5001</td>
<td><em>Emblica officinalis</em>, <em>Gymnema sylvestre</em>, <em>Momordica charantia</em>, <em>Pterocarpus marsupium</em>, <em>Syzygium cumini</em>, <em>Terminalia bellerica</em>, <em>Terminalia chebula</em></td>
<td>Alloxan-induced diabetic rats; feeding of 300 or 600 mg/kg daily for 15 d</td>
<td>At 600 mg/kg: ↓FBG (40%) ↓HbA1c (20%) ↓Hepatic glycogen (129%) ↓AST ↓ALT ↓Oxidative stress (pancreas) ↓Histological damage in the pancreas ↓Epinephrine-induced hyperglycemia</td>
<td>Glibenclamide (4 mg/kg): ↓FBG (41%) ↓HbA1c (24%) ↓Hepatic glycogen (139%) ↓AST ↓ALT ↓Histological damage in the pancreas ↓Epinephrine-induced hyperglycemia</td>
</tr>
<tr>
<td>Author(s)</td>
<td>Polyherbal preparation name</td>
<td>Herbal constituents</td>
<td>Study design</td>
<td>Effects of polyherbal preparation (% of change)</td>
<td>Effects of reference drug (% of change)</td>
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<tr>
<td>Yadav et al, 2007&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Diabegon</td>
<td>Aegle marmelos (leave), Asfetum punjabinum, Berberis aristata (tuber/root), Citrulus colocynthis (root), Curcuma longa (tuber/root), Cyperus rotundous (root), Embelia officinalis (fruit), Eugena jambolana (fruit), Gymnema sylvestre (leave), Momordica charantia (fruit), Piper longum (fruit/root), Pterocarpus marsupium (leave), Plumbago zeylanica (root), Swertia chirata (leave), Terminalia balaerica (fruit), Terminalia chebula (fruit), Trigonella foenum-graecum (fruit), Zingiber officinale (tuber)</td>
<td>High fructose diet-fed rats; feeding of 100 mg/kg daily for 56 d</td>
<td>↓FBG (36%)</td>
<td>Rosiglitazone (60 µg/kg): ↓FBG (11%)</td>
</tr>
<tr>
<td>Thakkar et al, 2010&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Glyoherb</td>
<td>Aragyavardhini, Azadirachta indica, Bang bhasma, Curcuma longa, Chanpraphba, Devdar, Gymnema sylvestre, Harde, Holarrhena antidiysenterica, Mahameiva, Momordica charantia, Phyllanthus emblica, Psidium guajava, Saurops androgynus, Swertia chirata, Tribulus terrestris, Trigonella foenum-graecum</td>
<td>STZ-induced diabetic rats; feeding of 200–600 mg/kg daily for 28 d</td>
<td>At 600 mg/kg: ↓FBG (75%)</td>
<td>Glibenclamide (5 mg/kg): ↓FBG (69%)</td>
</tr>
<tr>
<td>Gautam et al, 2013&lt;sup&gt;16&lt;/sup&gt;</td>
<td>HAL</td>
<td>Momordica charantia (fruit), Trigonella foenum-graecum (seed), Withania somnifera (root)</td>
<td>STZ-induced diabetic rats; feeding of lyophilized hydroalcoholic extract (250–1 000 mg/kg) for 21 d</td>
<td>At 500 mg/kg: ↓FBG (52%)</td>
<td>Metformin (500 mg/kg): ↓FBG (55%)</td>
</tr>
</tbody>
</table>
Table 1 (continuation 2)  Polyherbal formulations that have been tested in animal studies for management of diabetes

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Polyherbal preparation name</th>
<th>Herbal constituents</th>
<th>Study design</th>
<th>Effects of polyherbal preparation (% of change)</th>
<th>Effects of reference drug (% of change)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yadav et al, 2013[17]</td>
<td>MAC-ST/001</td>
<td>Azadirachta indica (seed), Caesalpinia bonducella (seed), Momordica charantia (fruit), Syzygium cumini (seed), Trigonella foenum-graecum (seed)</td>
<td>STZ-induced diabetic rats; feeding of 100–400 mg/kg daily for 20 d</td>
<td>At 400 mg/kg: ↓FBG (51%) ↓TC (39%) ↓BUN (58%) ↓Creatinine (38%) ↓ALT ↓AST ↓ALP ↓Histological damage in the pancreas</td>
<td>Glibenclamide (10 mg/kg): ↓FBG (47%) ↓TC (42%) ↓BUN (60%) ↓Creatinine (35%) ↓ALT ↓AST ↓ALP ↓Histological damage in the pancreas</td>
</tr>
<tr>
<td>Kesavanarayanan et al, 2013[18]</td>
<td>DIA-2</td>
<td>Allium sativum (bulb), Lagerstroemia speciosa (leaf)</td>
<td>High-fat diet/low-dose STZ-induced type 2 diabetic rats; feeding of 62.5–500 mg/kg daily for 14 d</td>
<td>At 125 mg/kg: ↓FBG (60%) ↑Insulin (39%) ↓TC (≈70%) ↓TG (≈80%)</td>
<td>Rosiglitazone (8 mg/kg): ↑FBG (60%) ↑Insulin (11%) ↓TC (≈60%) ↓TG (≈60%)</td>
</tr>
<tr>
<td>Chan et al, 2009[19]</td>
<td>SR10</td>
<td>Radix Astragali (root), Radix Codonopsis (root), Cortex Lycii (root)</td>
<td>db/db type 2 diabetic mice; feeding of 464 or 927 mg/kg once daily for 4 weeks</td>
<td>At 927 mg/kg: No significant effect on glucose tolerance ↓FBG (22%) ↑Insulin (36%) ↑Antioxidant defense (plasma and liver)</td>
<td>Metformin (200 mg/kg): ↑Glucose tolerance The effect of metformin has not checked for other parameters.</td>
</tr>
<tr>
<td>Joshi et al, 2007[20]</td>
<td>Diakyur</td>
<td>Cassia auriculata, Cassia javanica, Gymnema sylvestre, Mucuna pruriens, Salacia reticulate, Syzygium jambolanum, Terminalia arjuna</td>
<td>Alloxan-induced diabetic rats and rabbits; feeding of 1 600 mg/kg daily for 28 d</td>
<td>↓FBG (rat: 26%, rabbit: 30%) ↑Glucose tolerance ↓Oxidative stress (plasma, erythrocyte, liver, kidney)</td>
<td>Glibenclamide (2 mg/kg): ↓FBG (rat: 30%, rabbit: 33%) The effect of glibenclamide has not checked for other parameters.</td>
</tr>
<tr>
<td>Bangar et al, 2009[21]</td>
<td>Karnim Plus</td>
<td>Azadirachta indica, Momordica charantia, Ocimum sanctum, Picrorhiza kurroa, Zingiber officinale</td>
<td>Alloxan-induced diabetic rats; feeding of 200 or 400 mg/kg daily for 11 d</td>
<td>At 400 mg/kg: ↓FBG (19%) ↓Urea (11%) ↓Creatinine (21%) ↓TC (37%)</td>
<td>Glibenclamide (4 mg/kg): ↓FBG (52%) ↓Urea (61%) ↓Creatinine (33%) ↓TC (50%)</td>
</tr>
</tbody>
</table>
Table 1 (continuation 3) Polyherbal formulations that have been tested in animal studies for management of diabetes

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Polyherbal preparation name</th>
<th>Herbal constituents</th>
<th>Study design</th>
<th>Effects of polyherbal preparation (% of change)</th>
<th>Effects of reference drug (% of change)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Katiyar et al, 2012[22]</td>
<td>—</td>
<td>Azadirachta indica (leave), Gymnema sylvestre (leave), Momordica charantia (fruit), Syzygium cumini (seed), Trigonella foenum-graecum (seed)</td>
<td>Alloxan-induced diabetic rats; feeding of 500 mg/kg once a day for 4 weeks</td>
<td>↓FBG (≈60%) ↓Oxidative stress ↑Antioxidant defense (kidney)</td>
<td>Glibenclamide: ↓FBG (≈58%) ↓Oxidative stress ↑Antioxidant defense (kidney)</td>
</tr>
<tr>
<td>Lanjhiyana et al, 2011[23]</td>
<td>SEPHF</td>
<td>Aegel marmelos (root), Aloe vera (leave), Elaeodendron glaucum (leave), Murraya koenigii (root), Pongamia pinnata (stem bark)</td>
<td>Alloxan-induced diabetic rats; feeding of 50-200 mg/kg for 21 d</td>
<td>At 200 mg/kg: ↓FBG (≈50%) ↑Insulin (59%) ↓HbA(_{1c}) (71%) ↓TC (32%) ↓TG (31%) ↓LDL (49%) ↑HDL (83%) ↓ALT ↓AST ↓ALP ↓Oxidative stress ↓Histological damage in the pancreas No significant effect on urea and creatinine</td>
<td>Tolbutamide (250 mg/kg): ↓FBG (≈60%) ↑Insulin (55%) ↓HbA(_{1c}) (52%) ↓TC (28%) ↑TG (27%) ↓LDL (58%) ↑HDL (83%) ↓ALT ↓AST ↓ALP ↓Oxidative stress ↓Histological damage in the pancreas No significant effect on urea and creatinine</td>
</tr>
<tr>
<td>Akhtar et al, 2012[24]</td>
<td>Ziabeen</td>
<td>Aloe barbadensis, Azedarachta indica, Eugenia jambolana, Gymnema sylvestre, Momordica charantia, Holarrhena antidysenterica, Piper nigrum, Swertia chirata,</td>
<td>Alloxan-induced diabetic rabbits; feeding of 2-4 g/kg at single dose or once a day for 30 d</td>
<td>At 4 g/kg: ↑Glucose tolerance ↑Body weight at day 30 (26%) ↓FBG at day 30 (56%)</td>
<td>Pioglitazone (1 mg/kg): No significant effect on glucose tolerance ↓FBG at day 30 (3%)</td>
</tr>
</tbody>
</table>

ALP: alkaline phosphatase; ALT: alanine transaminase; AST: aspartate transaminase; BUN: blood urea nitrogen; FBG: fasting blood glucose; HbA\(_{1c}\): glycosylated hemoglobin; HDL: high-density lipoprotein; LDL: low-density lipoprotein; PPAR: peroxisome proliferator-activated receptor; STZ: streptozotocin; TC: total cholesterol; TG: triglyceride; VLDL: very low-density lipoprotein; ↑: increase; ↓: decrease; ≈: approximately equal to.
<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Polyherbal formulation name</th>
<th>Herbal constituents</th>
<th>Study design</th>
<th>Effects of polyherbal preparation (% of change)</th>
<th>Effects of reference drug (% of change)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ismail Khan et al, 2012[39]</td>
<td>—</td>
<td>Eugenia jambolana (seed), Gymnema sylvestre (leave), Momordica charantia (fruit), Mucuna pruriens (seed), Trigonella foenum graecum (seed), Withania somnifera (root)</td>
<td>93 patients with T1DM were administered 1 or 1.5 g of polyherbal compound three times a day for 12 weeks</td>
<td>At 1.5 g: ↓FBG (38%), ↓PPBG (43%), ↓HbA1c (21%), ↓Insulin (19%), ↓HOMA (52%)</td>
<td>No significant effect on AST, ALT, ALP, urea and creatinine</td>
</tr>
<tr>
<td>Kant et al, 2002[40]</td>
<td>Diabecon (D-400)</td>
<td>Asparagus racemosus, Balsamodendron mukul, Eugenia jambolana, Gymnema sylvestre, Momordica charantia, Ocimum sanctum, Pterocarpus marsupium</td>
<td>30 diabetic patients with retinopathy were administered 2 tablets three times a day for 3 months</td>
<td>Diabecon was effective for retinopathy (↓haemorrhages, ↓micro-aneurysm, ↓exudation, ↓retinitis proliferans)</td>
<td>—</td>
</tr>
<tr>
<td>Yajnik et al, 1993[41]</td>
<td>Diabecon (D-400)</td>
<td>Asparagus racemosus, Balsamodendron mukul, Eugenia jambolana, Gymnema sylvestre, Momordica charantia, Ocimum sanctum, Pterocarpus marsupium</td>
<td>43 patients with T1DM and T2DM were administered 2 tablets twice daily for 2 weeks</td>
<td>↓FBG (31%), ↓PPBG (33%)</td>
<td>—</td>
</tr>
<tr>
<td>Viswanathan et al, 2011[42]</td>
<td>—</td>
<td>Aloe vera, Cocos nucifera, Curcuma longa, Glycyrrhiza glabra, Musa paradisical, Pandanus odoratissimus</td>
<td>20 patients with T2DM and foot ulcers were treated with the polyherbal cream for 5 months</td>
<td>↓Length of wound (32%), ↓Width of wound (33%)</td>
<td>Silver sulphadiazine: ↓Length of wound (35%), ↓Width of wound (37%)</td>
</tr>
<tr>
<td>Said et al, 2008[43]</td>
<td>Glucolevel</td>
<td>Atriplex halimus (leave), Juglans regia (leave), Olea europea (leave), Urtica dioica (leaf)</td>
<td>16 patients with T2DM were treated with 1 tablet three times a day for 4 weeks</td>
<td>↓FBG (27%), ↓HbA1c (18%)</td>
<td>—</td>
</tr>
</tbody>
</table>

ALP: alkaline phosphatase; ALT: alanine transaminase; AST: aspartate transaminase; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin; HOMA: homeostasis model assessment-estimated insulin resistance; PPBG: postprandial blood glucose; T1DM: type-1 diabetes mellitus; T2DM: type-2 diabetes mellitus; ↑: increase; ↓: decrease.
G. sylvestre, T. foenum-graecum, Curcuma longa and Syzygium cumini were most commonly used in the tested herbal products. For example, M. charantia, G. sylvestre and T. foenum-graecum exists in 11, 9 and 8 of the products, respectively. M. charantia (Karela, bitter melon, bitter gourd) has passed several animal and clinical studies, developing a reputation of effectiveness in treatment of diabetes[3]. Administration of M. charantia fruits or seeds to T1DM and T2DM patients significantly decreased FBG, postprandial blood glucose (PPBG) and HbA1c levels[44-48]. Further, it has been shown that M. charantia was more effective in the management of serum glucose, lipids and diabetes-related complications (retinopathy and myocardial infarction) than rosiglitazone[49]. Another effective herb is T. foenum-graecum. Treatment with its seeds facilitated the management of diabetes in more than 25 animal studies[5]. Several clinical trials have also shown hypoglycemic and hypolipidemic effects of T. foenum-graecum in diabetic patients[5,50]. Finally, several studies have shown that G. sylvestre (Gurmar) can improve glycemic control in diabetes. According to clinical trial reports, in diabetic patients taking its extract as a supplement, G. sylvestre decreased FBG, PPBG, HbA1c, and serum lipids enough that the dosage of oral hypoglycemic drugs could be decreased[51-53].

4 Future prospective of polyherbal formulations

It is likely that the increasing awareness of the effectiveness of herbal medicines, coupled with a similar growing understanding of the side effects of synthetic drugs will lead to an increase in patient’s interest in alternative and herbal therapy[54]. Phytochemical products with potent hypoglycemic and hypolipidemic properties are already promising approaches for management of diabetes and reducing its complications, particularly cardiovascular events. The adoption of alternative strategies need not to be strictly at the expense of synthetic medicines. For example, diabetes has multifactorial pathogenicity and requires multi-modal management approach. Therefore, successful future therapeutic strategies for diabetes will feature the combination of various agents from different medical traditions[55]. It is believed that herbal formulations containing multiple plants have synergistic, or potentiative effects enhancing the desired actions. However, components of a polyherbal formulation may also have actions that are antagonistic to the desired pharmacological outcomes. Thus, an extensive research effort is needed to develop the best mixture from various antidiabetic plants to produce maximum therapeutic efficacy with minimum side effects. Further, although numerous phytochemicals have been suggested for management of blood glucose and lipids, the number of clinical trials supporting their benefit to diabetic patients is currently insufficient to make strong treatment recommendations. So, further well-designed clinical studies that evaluate diabetic outcomes and complications are needed to explore the efficacy of current drug candidates. Moreover, herbal medicines are not free from side effects and most of the products on the market today have not been subjected to drug approval process to verify their safety. Consequently, the standardization of a process for evaluation of safety and therapeutic risk/benefit associated with the use of a polyherbal formulation is an area that will require substantial attention. One more difficulty is that many clinicians are still somewhat unfamiliar with scientific name, pharmacodynamic and precise dosage of herbal products[56]. Further works on all of these topics is necessary.

5 Conclusions

Since diabetes is progressing unabatedly, there is an urgent need for finding new remedies. Chronic hyperglycemia leads to glycation of body proteins that in turn causes secondary complications affecting the cardiovascular system, eyes, kidneys and nerves[3]. It has been shown repeatedly that early onset of complications of diabetes can be delayed by controlling blood glucose. However, multifactorial metabolic diseases, like diabetes, require multi-drug regimens consisting of medications from different classes to prevent their complications. Use of polyherbal formulations may overcome this problem and help to prevent related complications. Data from animal studies show that the polyherbal formulations can reduce serum glucose and lipid levels as well as increase insulin and glucose tolerance in diabetic rodents. They also decrease oxidative stress in different tissues, such as the liver, kidney and pancreas, indicating that these formulations inhibit oxidative damage and may reduce the late complications of diabetes. Although only a small number of clinical trials have tested polyherbal formulations for use against diabetes, the initial results are encouraging and have confirmed their efficacy for managing blood glucose, retinopathy and foot ulcers. Fortunately, many diabetic patients are looking for alternative and herbal therapy and this demand may present an opportunity for clinicians to help their patients using polyherbal compounds. Nevertheless, much remains to be learned about long-term safety, toxicity and adverse effects of polyherbal preparations. Finally, well-planned long-term studies on these topics are needed to understand bioavailability, pharmaceutokinetics, drug interactions and ideal dosages of herbal products.

6 Acknowledgements

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7 Declarations of any conflicts of interest

The author has no other relevant affiliations or financial involvement with any other organization.
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